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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/806,645	07/12/2001	Yuri Kolesnikov	830010-2006.	3048

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EXAMINER	
WELLS, LAUREN Q	
ART UNIT	PAPER NUMBER
1617	17

DATE MAILED: 09/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/806,645	KOLESNIKOV ET AL.	
	Examiner	Art Unit	
	Lauren Q Wells	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,7-9 and 13-17* is/are pending in the application.

4a) Of the above claim(s) *4,13 and 17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7-9 and 14-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *14* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1, 4, 7-9, 13-17 are pending. Claims 4, 13 and 17 are withdrawn from consideration, as they are directed to non-elected subject matter. The Amendment filed 4/21/03, Paper No. 15, amended claims 1, 9, 14-16 and cancelled claims 2-3, 5-6, 10-12, and 18. The Amendment filed 7/24/03, Paper No. 16, amended claims 1 and 9.

Applicant's arguments with respect to the rejection of claims 1, 5, 7-9, 14-16 under 35 USC 103 have been considered but are moot in view of the new ground(s) of rejection. However, to the extent that the arguments may be relevant to the instant rejection, the Examiner will address them. See below.

Applicant's amendments to the claims filed 4/21/03 and 7/24/03, are sufficient to overcome the 35 USC 112, 1st and 2nd paragraph, rejections in the previous Office Action.

The 37 CFR 1.131 Declaration filed 4/21/03, is persuasive to overcome any art rejection that would have been made over US 6,008,258.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 9, 14, 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gevirtz et al. (5,635,204) in view of Nelson et al. (5,840,731) and in view of Needham et al. (6,261,582).

The instant invention is directed toward a composition comprising ketamine and morphine and a pharmaceutically acceptable topical excipient and a method of providing analgesia to a mammal comprising topically administering an effective dose of ketamine in combination with morphine.

Gevirtz et al. teach a method for transdermal induction of anesthesia, analgesia or sedation by simultaneously, transdermally administering fentanyl, an alpha adrenergic agonist, and ketamine. Disclosed is a method of inducing anesthesia comprising transdermally administering via a transdermal patch to the skin an amnesia producing drug selected from scopolamine, ketamine, and benzodiazepines, and after an amnesic state is produced, transdermally administering amounts of clonidine and fentanyl. Exemplified in the patches are carriers. Thus, the instant invention and Gevirtz et al. both teach a composition comprising an NMDA receptor antagonist (ketamine), an analgesic (fentanyl), and an excipient/carrier (polyisobutylene), and a method of applying the composition to the skin. See Example 1; Col. 5, line 35-Col. 6, line 50. The reference lacks morphine and the percent weight of ketamine based on the total weight of ketamine and morphine.

Nelson et al. teach a method and apparatus for administering analgesics. Fentanyl and morphine are disclosed as interchangeable analgesics that act on opiod pain receptors. See Col. 4, lines 11-42.

Needham et al. teach surgical methods and compositions thereof. Fentanyl and morphine are disclosed as interchangeable and combinable analgesics. See Col. 2, lines 60-64; Col. 15, lines 24-26.

It would have been obvious to one of ordinary skill in the art at the time the invention

was made to substitute the fentanyl of Gevirtz et al. for morphine because a) Gevirtz et al., Nelson et al, and Needham et al. are all directed to analgesic compositions; b) Nelson et al. and Needham et al. teach morphine and fentanyl as interchangeable opiod pain receptor analgesics; thus, one of ordinary skill in the art would be motivated to substitute morphine for fentanyl in the compositions of Gevirtz et al. because of the expectation of producing similar analgesic effects via the opiod pain receptor.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to teach the ketamine of the combined references as comprising 0.1-5% of the total weight of ketamine and morphine because it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. In re Aller, 105 USPQ 233.

Regarding claims 1, 7-8, it is respectfully pointed that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). In the instant case, the intended use does not result in a structural difference.

The claims are directed to a method of providing peripheral analgesia and not central or system analgesia to a mammal and a method of providing a tolerance attenuating analgesia to a mammal with pre-existing tolerance to an analgesic comprising topically administering a

composition comprising a tolerance-attenuating dose of ketamine in combination with morphine. Any properties exhibited by or benefits provided the composition are inherent and are not given patentable weight over the prior art. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties Applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. The burden is shifted to Applicant to show that the prior art product does not inherently possess the same properties as instantly claimed product. The prior art teaches application to the skin of compositions containing the same components as instantly claimed, which would inherently provide peripheral analgesia and not central or system analgesia as instantly claimed. Applicant has not provided any evidence of record to show that the prior art compositions do not exhibit the same properties as instantly claimed.

It is further respectfully pointed out that a compound and its properties are inseparable and since morphine is administered by the above prior art in the same way as that in the instant invention, the morphine of the prior art functions through the peripheral opiate receptor.

Claims 7-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gevirtz et al. in view of Nelson et al. and Needham et al. as applied to claims 1, 9, 14 and 15 above, and further in view of Kaneko et al (Anesthesiology '94).

Gevirtz et al., Nelson et al., and Needham et al. are applied as discussed above. The reference lacks a local anesthetic.

Kaneko et al. teach the synergistic antinociceptive interaction after epidural coadministration of morphine and lidocaine. See background.

It would have been obvious to one of ordinary skill in the art at the time the invention

was made to add the lidocaine of Kaneko et al. to the composition of the combined references because of the expectation of achieving synergistic analgesia, and hence, enhanced pain relief.

Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gevirtz et al. in view of Nelson et al. and Needham et al. as applied to claims 1, 9, 14 and 15 above, and further in view of Smith et al. (6,194,000)

Gevirtz et al., Needham et al., and Nelson et al. are applied as discussed above. The references lack a kit.

Smith et al. teach analgesic compositions comprising NMDA receptor antagonist. Disclosed are kits which comprise a plurality of unit dosage forms, in a container, the container including indicia indicative of a dosage regime. See abstract; Col. 9.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to teach the transdermal patches of the combined references in the kits of Smith et al. because a) the combined references and Smith et al. are both directed to analgesic compositions comprising NMDA receptor antagonists, such as ketamine, and Smith et al. teach that kits can comprise a plurality of unit dosage forms indicative of a dosage regime; thus, one of skill in the art would be motivated to teach the patches of the combined references in kits because of the expectation of achieving a product that is specialized in different dose amount for different dosage regimes.

Response to Arguments

Applicant argues, "Claim 14 provides for peripheral analgesia that is not suggested by Gervitz et al. in view of Nelson et al. and Needham et al.". This argument is not persuasive. The claims are directed to a method of providing to a mammal comprising topically administering a

composition comprising a tolerance-attenuating dose of ketamine in combination with morphine. Any properties exhibited by or benefits provided the composition are inherent and are not given patentable weight over the prior art. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties Applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. The burden is shifted to Applicant to show that the prior art product does not inherently possess the same properties as instantly claimed product. The prior art teaches application to the skin of compositions containing the same components as instantly claimed, which would inherently provide peripheral analgesia and not central or system analgesia as instantly claimed. Applicant has not provided any evidence of record to show that the prior art compositions do not exhibit the same properties as instantly claimed.

In summary, it is respectfully pointed out that since the prior art teaches the same combination of ingredients is administered in the same fashion as that of the instant method claims, then the methods are the same. It is furthermore respectfully pointed out that these arguments are not persuasive for the instant composition claims, wherein the intended use of the composition is not afforded patentable weight. It is respectfully pointed out that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). In the instant case, there is no structural difference.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lauren Q Wells whose telephone number is (703) 305-1878. The examiner can normally be reached on M-F (7-4:30), with alternate Mondays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (703)305-1877. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

lqw

SREENI PADMANABHAN
PRIMARY EXAMINER 9/13/03